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Original Research Article

A Comparative Analysis of Fracture Risk in Type 2 Diabetes Mellitus with That of Healthy Adults

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Abstract

Introduction: T2DM causes high blood glucose owing to insulin resistance or inadequate production. It now affects 9.3% of the world's population and is projected to reach 10.9% by the year 2045. The risks of cardiovascular disease, neuropathy, retinopathy, and an increased vulnerability to fractures, even in those with adequate bone density, are sequelae of type 2 diabetes. Population comparisons inform personalised therapies and better healthcare policy.

Aim and objectives: The goal is to compare fracture risk between Type 2 Diabetes Mellitus patients and healthy persons to understand better how diabetes affects bone health.

Method: The National Institute of Medical Sciences and Research in Jaipur compared trauma/fracture patients aged 40-80 with diabetes from July 2022 to December 2023. We gathered information on their demographics, way of life, and health, as well as their bone density and fracture risk, using individualised FRAX models. The study seeks to understand how diabetes affects bone health and identify fracture risk factors in diabetics.

Result: People with Type 2 DM (Group A) and those without the disease (Group B) are compared in this research. Group A, consisting of individuals aged 40–50, had lower levels of BMD (P=0.022) and HbA1c (P=0.041) compared to Group B. Significant differences (P=0.011) exist in the history of parental fractures. Despite the lack of statistical significance in the FRAX scores (P=0.054), numerical differences indicate possible clinical consequences that need more exploration.

Conclusion: Considering similar bone density and extensive osteoporosis therapy, diabetics, particularly those with comorbidities, have increased fracture risk.

Keywords: type-2 Diabetes, Fracture, Bone Health, Cardiovascular Risk.

Introduction

Type 2 diabetes mellitus, a chronic metabolic condition, involves elevated blood glucose levels due to insulin resistance or insufficient insulin production. Factors like obesity, sedentary habits, family history, and specific ethnic backgrounds elevate the risk. This complex disorder presents diverse manifestations due to disruptions in insulin action or secretion, affecting carbohydrate, fat, and protein metabolism. Prolonged high blood sugar levels contribute to microvascular and macrovascular complications, significantly impacting morbidity and mortality. As a key diagnostic marker, hyperglycemia signifies diabetes onset [1].

In 2019, about 9.3% of the global population, approximately 463 million individuals, grappled with Type 2 Diabetes Mellitus (T2DM). Forecasts predict a surge to 10.2% (578 million) by 2030 and a further climb to 10.9% (700 million) by 2045. Urban regions and high-income nations report higher prevalence rates compared to their rural and low-income counterparts [2].

Metabolic shifts and complications intertwined with type 2 diabetes mellitus (T2DM) encompass multifaceted impacts. T2DM presents potential low blood sugar scenarios, particularly with insulin or sulfonylurea usage, heightening the risk of adverse glucose dips. Hypertension commonly accompanies T2DM, amplifying cardiovascular risk landscapes. T2DM disrupts lipid profiles, leading to heightened triglycerides and reduced high-density lipoprotein (HDL) cholesterol levels, increasing the vulnerability to heart diseases. Peripheral neuropathy, arising from T2DM, induces extremity numbness, tingling, and severe pain, sometimes necessitating amputation. T2DM intricately affects

ocular blood vessels, fostering diabetic retinopathy and the potential for vision loss if left unmanaged [3,4].

Fracture risk in individuals with type 2 diabetes mellitus (T2DM) showcases an elevated likelihood of bone fractures compared to the general population. This augmented risk stems from various factors, including compromised bone quality, altered bone metabolism, and an increased susceptibility to falls. Notably, despite often retaining normal bone mineral density (BMD), individuals with T2DM might face compromised bone quality. Consequently, relying solely on BMD assessments may prove inadequate for evaluating fracture risk in T2DM patients. Incorporating an evaluation of bone quality alongside factors like age, duration of diabetes, and insulin therapy becomes crucial for a comprehensive assessment of fracture risk in T2DM individuals [5-11].

The intricate mechanisms underpinning bone fragility in type 2 diabetes mellitus (T2DM) are multifaceted. Several factors converge to heighten this vulnerability, including a disruption in bone turnover marked by reduced formation and heightened resorption. T2DM intricately alters bone microstructure and properties, diminishing bone strength and upping the risk of fractures. The accumulation of advanced glycation end-products (AGEs) due to chronic hyperglycemia affects collagen integrity, fosters marrow adiposity, and fuels inflammation, all detrimentally impacting bone health. Insulin resistance and hyperinsulinemia, core features of T2DM, disrupt bone cell function, hindering bone formation. Concurrently, microvascular complications like diabetic nephropathy and retinopathy impede nutrient supply to bone tissue, further compromising bone remodeling and elevating fracture risk [12-17].

Understanding and comparing fracture risk between individuals with type 2 diabetes mellitus (T2DM) and healthy adults carries crucial significance. Numerous studies consistently reveal that those with T2DM face a notably elevated risk of fractures compared to their non-diabetic counterparts. This comparison aids healthcare providers in pinpointing and addressing the heightened risk among those with diabetes, enabling tailored preventive strategies that encompass lifestyle adjustments and targeted medications to bolster bone health. Moreover, this comparison sheds light on diabetes's substantial impact on bone health, emphasizing the need for comprehensive diabetes management to mitigate fracture risks. These comparative studies also unearth specific risk factors linked to increased fracture vulnerability in T2DM individuals, such as prolonged diabetes duration, low physical activity, and insulin therapy, guiding healthcare providers in risk assessment and intervention planning [8,18-20].

Fracture risks, notably hip fractures, prevail in individuals with type 2 diabetes mellitus (T2DM) despite seemingly normal or higher bone mineral density levels, a puzzle yet to be fully unraveled. The increased risk stems from multifaceted factors including elevated risks of falls, obesity-related concerns, sarcopenia, and various co-existing health issues. Furthermore, T2DM disrupts bone dynamics by decreasing turnover, impairing formation, and altering bone structure and properties, leading to bone fragility. Understanding the intricate impact of T2DM on bone health is pivotal, guiding accurate fracture risk assessments and tailoring effective management strategies [21-24].

Comparative analysis among diverse populations offers a window into the prevalence, risk factors, and management strategies surrounding type 2 diabetes mellitus (T2DM) and its complications, a crucial pathway yielding insights for improved healthcare. This approach allows identification of variations in complication prevalence and management across different groups, aiding tailored care strategies. For instance, comparing T2DM complications in Brazilian and Mexican adults showcased distinct risks, guiding targeted interventions. Such analysis illuminates common risk factors, guiding preventive measures. For example, screening strategies in disadvantaged areas revealed community-based approaches reaching high-risk groups more effectively. Furthermore, comparisons between treatment options, like metformin/glibenclamide combinations, inform superior control strategies. Overall, comparative analysis in T2DM care holds promise in customizing interventions, improving prevention, and enhancing treatment outcomes, shaping better healthcare policies and practices [25-27].

Method

Research Design

This comparative cross-sectional study was conducted in the Department of Orthopedics, National Institute of Medical Sciences and Research, Jaipur, Rajasthan. From July 2022 to December 2023, this study was conducted on patients with fractures attending the Department of Orthopedics. At the Orthopaedics OPD and Emergency Department of NIMS Hospital in Jaipur, this 18-month study examines 40-80-year-olds with trauma/fracture and diabetes mellitus. Subjects were assessed for demographics, medical history, lifestyle variables (such as smoking and alcohol use), and prescription usage. Height, weight, waist circumference (WC), and hip circumference (HC) were measured twice and averaged for accuracy (0.1 cm). Also measured were BMI and blood pressure. After overnight fasting, serum fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c), uric acid (UA), total cholesterol (TC), triglyceride (TG),

HDL-C, LDL-C, creatinine (Cr), serum calcium (Ca), and 25-hydroxyvitamin D3 (25 (OH)D3) were measured using automatic biochemical analyzers and mass spectrometry. The Hologic Sahara ultrasonic bone density densitometer and the Prodigy Advance DXA System were used to determine BMD, which correlated well with DEXA results. BMD status was classified according to the WHO standard, using T-scores (≥-1.0, -1.0--2.5, and ≤-2.5) to indicate normal density, osteopenia, and osteoporosis (OP). Fracture risk was assessed using FRAX models customized to the country's fracture epidemiology and mortality. Focusing on well-established and independent fracture risk factors, FRAX picked its risk factors for simplicity. FRAX has been criticized for ignoring exposure-response correlations. Although complex, FRAX does not account for different levels of exposure, such as the increased risk of fractures linked with glucocorticoid usage. This research seeks to investigate how diabetes mellitus affects bone health and identify fracture risk factors in the given patient demography.

Inclusion and Exclusion Criteria

Inclusion

- Trauma or fracture patients who took oral antidiabetic medications with or without insulin were categorized as having T2DM in the 40-80 age range.
- Trauma or fracture patients with DM after 40 who got insulin are unclassified.
- Nondiabetic 40-80-year-olds with trauma/ fracture.
- The patient has provided written authorization.

Exclusion

- Patients with cancer, alcoholism, HIV, RA, or metabolic disease.
- Polytraumatic, high-velocity injury patient.
- Patient with other pathological fractures.
- A person diagnosed with type 1 diabetes.

Statistical Analysis

Data was analysed using IBM-SPSS Statistics 23.3. For categorical data, frequency and percentage analyses were descriptive, whereas mean and standard deviation represented continuous variables. The chi-squared and t-tests analysed quantitative and qualitative data separately. Results were presented as means with SD. Significance was 0.05 (p-value) and extremely significant at 0.01.

Result

Table 1 shows Group A (Type 2 DM) and Group B (Non-diabetic) age, gender, and anthropometric characteristics. Significantly different age distributions exist across the groups (P=0.000), with a larger percentage of people in Group A falling into the 40–50 age bracket. The results show no significant difference between the sexes (P=0.641). When it comes to anthropometrics, there is no significant difference in weight (P=0.659), but there is a significant difference in height (P=0.001), with Group B persons averaging a higher height. Accordingly, the disparities between the Type 2 DM and non-diabetic groups may be attributable, in part, to variations in age and height.

Table 1: Age and Gender distribution of both the groups

Age group	**Group A: Type 2 DM**		**Group B: Non-diabetic**		**P value**
	No.	**%**	**No.**	**%**	
40-50	32	34.78%	33	35.87%	$\chi2$=80.590 P=0.000 (S)
50-60	31	33.70%	19	20.65%	
60-70	14	15.22%	14	15.22%	
70-80	12	13.04%	26	28.26%	
> 80	3	3.26%	0	0.00%	
Total	**92**	**100.0%**	**92**	**100.0%**	
Mean±SD	**57.40±11.490**		**58.89±13.140**		
Gender	**Group A: Type 2 DM**		**Group B: Non-diabetic**		**P value**
	No.	**%**	**No.**	**%**	
Male	59	64.1%	62	67.4%	$\chi2$=0.217 P=0.641 (NS)
Female	33	35.9%	30	32.6%	
Total	**92**	**100.0%**	**92**	**100.0%**	
	Group	**N**	**Mean**	**Std. Deviation**	**P value**
Weight	Group A: Type 2 DM	92	62.62	10.350	0.659 (NS)
	Group B: Non-diabetic	92	63.17	6.112	
Height	Group A: Type 2 DM	92	166.80	8.566	0.001 (S
	Group B: Non-diabetic	92	171.16	8.438	

Table 2 shows factor distribution in Group A (Type 2 DM) and Group B (Non-diabetic). Group B (17.60%) had a greater frequency of parental fracture than Group A (5.40%), with a significant P value of 0.011 (S). Other characteristics including age, smoking, steroid usage, rheumatoid arthritis, secondary osteoporosis, and alcohol use do not vary across groups. While parental fracture history varied considerably, other variables do not significantly affect bone health differences between Type 2 DM and non-diabetics.

Table 2: Alcohol status of both the groups

H/o parental fracture	**Group A: Type 2 DM**		**Group B: Non-diabetic**		**P value**
	No.	%	No.	%	
Yes	5	5.40%	16	17.60%	c2=6.504
No	87	94.60%	76	82.60%	P=0.011
Total	92	100.00%	92	100.00%	(S)
Group	**N**	**Mean**	**Std. Deviation**	**P value**	
Group A: Type 2 DM	92	22.611	3	0.057 (NS)	
Group B: Non-diabetic	92	21.753	3.073		
Smoking	**Group A: Type 2 DM**		**Group B: Non-diabetic**		**P value**
	No.	%	No.	%	
Yes	33	35.90%	26	28.30%	c2=1.223
No	59	64.10%	66	71.70%	P=0.269
Total	92	100.00%	92	100.00%	(NS)
Steroids used	**Group A: Type 2 DM**		**Group B: Non-diabetic**		**P value**
	No.	%	No.	%	
Yes	8	8.70%	3	3.30%	c2=2.417
No	84	91.30%	89	96.70%	P=0.120
Total	92	100.00%	92	100.00%	(NS)
Rheumatoid Arthritis	**Group A: Type 2 DM**		**Group B: Non-diabetic**		**P value**
	No.	%	No.	%	
Positive	4	4.30%	1	1.10%	c2=1.850
Negative	88	95.70%	91	98.90%	P=0.174
Total	92	100.00%	92	100.00%	(NS)
Secondary Osteoporosis	**Group A: Type 2 DM**		**Group B: Non-diabetic**		**P value**
	No.	%	No.	%	
Yes	6	6.50%	2	2.20%	c2=2.091
No	86	93.50%	90	97.80%	P=0.148
Total	92	100.00%	92	100.00%	(NS)
Alcohol	**Group A: Type 2 DM**		**Group B: Non-diabetic**		**P value**
	No.	%	No.	%	
Yes	24	26.10%	24	26.10%	c2=0.000
No	68	73.90%	68	73.90%	P=1.000
Total	**92**	**100.00%**	**92**	**100.00%**	(NS)

Figure 1 shows Group A (Type 2 DM) and Group B (Non-diabetic) BMD. Group A has a mean BMD of -1.809 and a standard deviation of 0.514, whereas Group B has -1.975 and 0.451. The P value of 0.022 demonstrates statistical significance (S), indicating a substantial BMD difference between groups. Group A Type 2 diabetics had a greater mean BMD than Group B non-diabetics. This suggests that Type 2 DM may affect bone health, requiring more study of the processes.

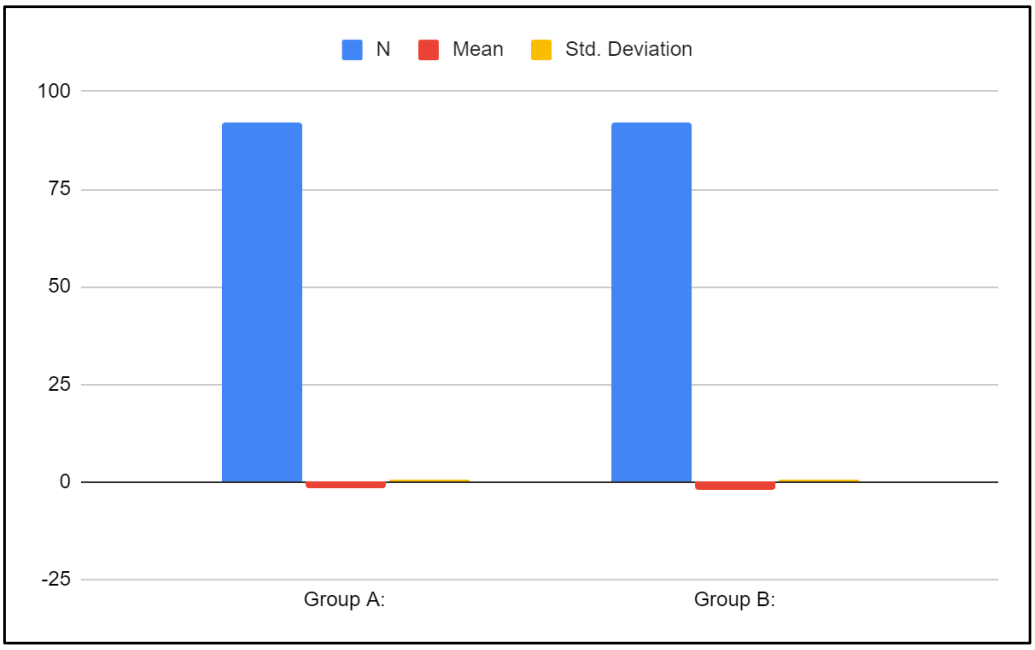

Figure 1: Bone Mineral Density of both the groups

Figure 2 shows Group A's (Type 2 DM) and Group B's (Non-diabetic) HbA1c values. Group A had a mean HbA1c of 6.221 and a standard deviation of 1.1798, whereas Group B had 6.601 and 1.3215. A P value of 0.041 shows statistical significance. The two groups had significantly different HbA1c values. Type 2 DM patients in Group A had lower HbA1c values than non-diabetics in Group B. This may help explain glycemic control in these people.

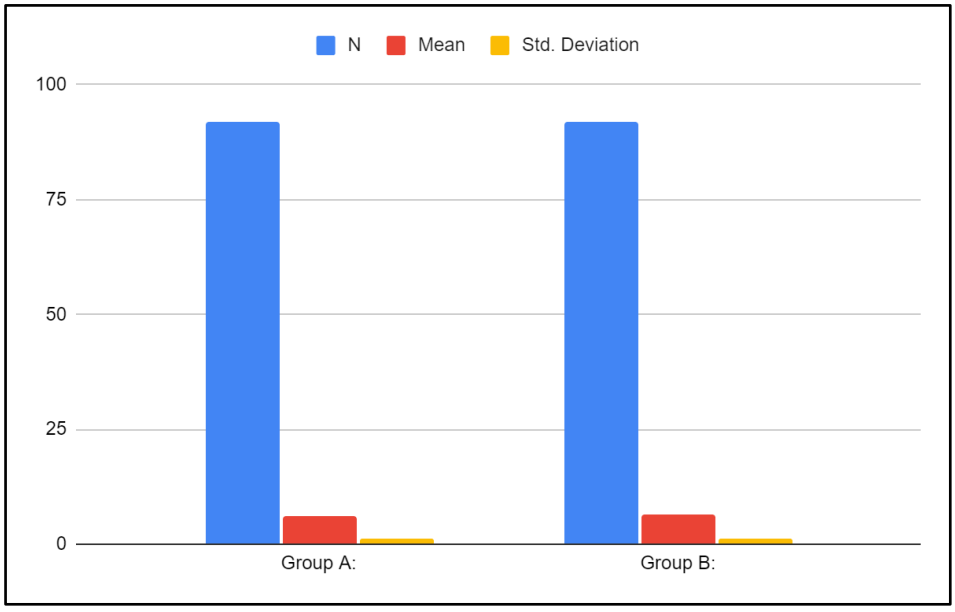

Figure 2: HbA1c of both the groups

Figure 3 shows Group A (Type 2 DM) and Group B (Non-diabetic) FRAX scores. Group A's mean FRAX score is 9.246 with a standard deviation of 7.1908, while Group B's is 7.314 with 6.2734. The P value (0.054) implies significance. Although not statistically significant, the numerical differences in mean scores suggest Group A may have higher FRAX scores than Group B. A bigger sample size or further research may be needed to assess the clinical implications of this pattern.

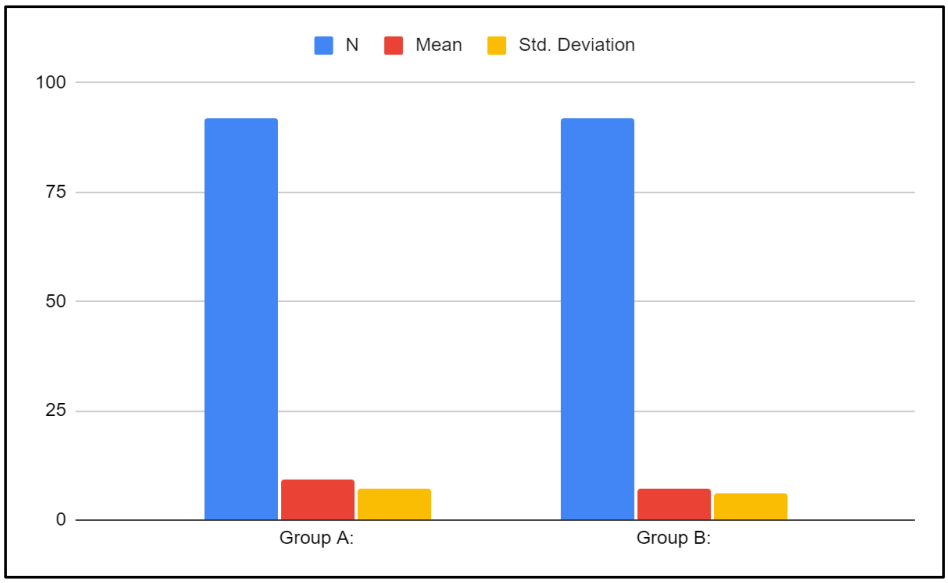

Figure 3: FRAX score of both the groups

Discussion

In a prospective cohort study by Li et al. (2019) involving 3,149 participants, 138 of whom had diabetes, we explored the relationship between frailty and fracture risk. Individuals with diabetes showed higher bone mineral density and frailty levels compared to non-diabetic individuals. The analysis revealed a significant association between frailty (measured by a Frailty Index) and the risk of fragility fractures, with hazard ratios of 1.02 and 1.19 for every 0.01 and 0.10 increase in the Frailty Index, respectively. Additionally, frailty intensified the impact of diabetes on fragility fractures, showing a higher risk of fractures in diabetic individuals [28].

In the Health, Aging, and Body Composition Study by Strotmeyer et al. (2005) involving 2,979 older adults (42% black) aged 70 to 79 years, we investigated the relationship between type 2 diabetes mellitus (DM) and fracture risk. Our findings revealed that individuals with DM had a 64% higher risk of fractures, even after accounting for hip bone mineral density (BMD) and other fracture risk factors. Interestingly, impaired fasting glucose didn't significantly correlate with fractures. Among those with DM, those who experienced fractures exhibited lower hip BMD and lean mass, alongside higher instances of reduced peripheral sensation, stroke history, decreased physical performance, and falls compared to diabetic individuals without fractures [18].

In a nationwide cohort study by Lee et al. (2023) encompassing 2,746,078 individuals with type 2 diabetes mellitus (T2DM), we scrutinized how body mass index (BMI) and T2DM influenced fracture risk across specific anatomical sites. Notably, underweight individuals with T2DM exhibited a heightened risk for total fractures (HR, 1.268; 95% CI, 1.228 to 1.309), especially vertebra fractures (HR, 1.896; 95% CI, 1.178 to 2.021), while those categorized as obese or morbidly obese showed a reduced risk for total fractures (HR, 0.891 and 0.873, respectively). This trend persisted for hip fractures, where underweight individuals with T2DM had the highest risk (HR, 1.896), contrasting sharply with the lower risk observed in obese (HR, 0.643) and morbidly obese groups (HR, 0.627). These findings underscore the varied association between BMI, T2DM, and fracture risk across different anatomical locations, particularly highlighting the heightened risk of hip fractures in individuals with T2DM [29].

In a comprehensive nationwide cohort study by Park et al. (2021) involving 5,761,785 individuals over 50 years old, our investigation sought to unravel the connection between type 2 diabetes mellitus (T2DM) and hip fractures in South Korea. The study meticulously categorized subjects based on their diabetes status, from prediabetes to various T2DM durations, and compared them with those without T2DM. The findings revealed compelling trends: the risk of hip fractures steadily rose along the spectrum of diabetes progression. Specifically, individuals in the prediabetes phase exhibited a slight elevation in hip fracture risk, while this risk substantially increased in newly-diagnosed T2DM cases and continued to escalate with longer diabetic durations. Notably, this trend persisted across genders and age groups (50-64 years, 65-74 years, and over 75 years). The robustness of this association was consistent and linear, indicating a direct correlation between the duration of T2DM and heightened hip fracture risk [30].

Individuals with type 2 diabetes mellitus (T2DM) face escalated fracture risks despite seemingly normal bone density due to various interconnected factors. Bone quality alterations, imbalances in remodeling, accumulation of advanced glycation

end-products, inflammation, and heightened fall risks contribute to this vulnerability. These intricate mechanisms underscore the complexity of fracture susceptibility in T2DM, demanding multifaceted preventive strategies [31-36].

Bone mineral density (BMD) serves as a standard measure for assessing fracture risk in type 2 diabetes mellitus (T2DM) and healthy adults. Yet, in T2DM individuals, higher BMD doesn't always align with reduced fracture risks, hinting at nuanced factors. Despite elevated BMD in T2DM, fracture occurrences persist, suggesting potential issues with bone quality, such as compromised microarchitecture and composition. This discrepancy unveils the insufficiency of BMD alone in gauging fracture risk in T2DM, as factors like inflammation and diabetes-specific risks could play pivotal roles. So, while BMD is vital, its sole reliance might overlook the complexities driving fractures in T2DM, emphasizing the need to integrate bone quality and T2DM-specific risks into assessments [37-39].

Highlighting heightened fracture risk in those with type 2 diabetes mellitus (T2DM) carries vital clinical implications, steering practice toward tailored strategies. Beyond bone mineral density (BMD) assessments, interventions should embrace multifaceted approaches, encompassing bone quality enhancements and falls prevention. Incorporating trabecular bone score (TBS) into screenings might refine risk assessments for T2DM-associated fractures. Moreover, leveraging antiresorptive therapies like bisphosphonates and denosumab, and considering osteoanabolic treatments such as teriparatide, could benefit those at heightened risk. By reshaping prevention strategies, screening protocols, and targeted interventions, we can address the fracture burden in this population, ultimately improving patient outcomes [40-43].

Conclusion

In conclusion, diabetics had a higher fracture risk despite intensive osteoporosis therapy and equivalent BMD. This tendency was especially true for diabetics with problems. The results emphasize the need for better fracture risk assessment, patient education, and medication usage, particularly as diabetes progresses. In this group, fracture risk must be addressed beyond typical osteoporosis care to account for diabetes-related comorbidities. This highlights the necessity of personalised and proactive fracture risk mitigation strategies in diabetics, improving patient outcomes and healthcare management.

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